Attorney's Docket No.: 09744-006001 / DITI 107

Applicant: Richard T. DEAN et al.

Serial No.: 08/236,402 Filed: May 2, 1994



CLAIMS

1. (amended) A reagent for preparing a scintigraphic imaging agent comprising a specific binding compound having a molecular weight of less that 10,000 daltons, the compound being covalently linked to a radiolabel complexing moiety having a formula selected from the group consisting of:

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 R^1 —CO— $(amino acid)^1$ – $(amino acid)^2$ —Z

wherein

(amino acid)¹ and (amino acid)² are each independently any primary α - or β - amino acid that does not contain a thiol group;

Z is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoethylamine and 3-mercaptopropylamine;

 R^1 is lower (C^1 – C^4) alkyl or a covalent linkage to the compound;

wherein when Z is cysteine, homocysteine, isocysteine or penicillamine, Z comprises a carbonyl group covalently linked to a hydroxyl group, a NR^3R^4 group wherein R^3 and R^4 are each independently H or lower (C^1-C^4) alkyl, an amino acid, or a peptide comprising 2 to 10 amino acids,

and

Y—(amino acid)¹—NHR²

wherein

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Y is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoacetate and 3-mercaptopropionate;

(amino acid)¹ and (amino acid)² are each independently any primary α - or β - amino acid that does not contain a thiol group;

 R^2 is selected from the group consisting of H, a lower (C^1-C^4) alkyl, and a covalent linkage to the compound;

wherein when Y is cysteine, homocysteine, isocysteine or penicillamine, Y comprises an amino group covalently linked to-H, an amino acid, or a peptide comprising 2 to 10 amino acids; and

wherein the moiety is linked to the compound through R¹, R², a sidechain group of (amino acid)², an amino group of cysteine, homocysteine, isocysteine, or penicillamine, or a carboxyl group of cysteine, homocysteine, isocysteine or penicillamine.

2. (amended) The reagent of claim 1 wherein the radiolabel complexing moiety is selected from the group consisting of

and

(mercaptocarboxylic acid)—(amino acid)¹—(amino acid)²,

wherein

(amino acid)¹ and (amino acid)² are each independently any primary α - or β -amino acid;

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(amino thiol) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoethylamine, and 3-mercaptopropylamine, and (mercaptocarboxylic acid) is selected from the group consisting of cysteine, isocysteine, homocysteine, penicillamine, 2-mercaptoacetic acid,

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3. (amended) The reagent of Claim 2 wherein the radiolabel complexing moiety is selected from the group consisting of –Gly-Gly-Cys- and Cys-Gly-Gly-.

and 3-mercaptopropionic acid.

- 5. (amended) A reagent according to Claim 1 wherein the compound is a peptide comprising 4 to 100 amino acids.
- 6. (amended) The reagent of Claim 5 wherein the peptide and the moiety are linked through one or more amino acids.
- 7. A scintgraphic imaging agent comprising the reagent according to Claim 1 wherein the radiolabel binding moiety is bound to a radiolabel.
 - 8. The reagent of Claim 7 wherein the radiolabel is technetium-99m.
- 11. A complex formed by reacting the reagent of Claim 1 with technetium-99m in the presence of a reducing agent.
- 12. The complex of Claim 11, wherein the reducing agent is selected from the group consisting of a dithionite ion, a stannous ion and a ferrous ion.
- 13. A complex formed by labeling the reagent of Claim 1 with technetium-99m by ligand exchange of a prereduced technetium-99m complex.

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14. A kit for preparing a radiopharmaceutical preparation, said kit comprising a sealed vial containing a predetermined quantity of the reagent of Claim 1 and a sufficient amount of reducing agent to label the reagent with technetium-99m.

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- 15. A method for labeling a reagent according to Claim 1 comprising reacting the reagent with echnetium-99m in the presence of a reducing agent.
- 16. The method of Claim 15, wherein the reducing agent is selected from the group consisting of a dithionite ion, a stannous ion and a ferrous ion.
- 17. A method for imaging a site within a mammalian body comprising administering an effective diagnostic amount of the reagent of Claim 2 and detecting a radioactive signal from the technetium-99m localized at the site.
- 19. (amended) The reagent of Claim 5 wherein the peptide comprises a linear peptide or a cyclic peptide.
- 20. (amended) The reagent of Claim 1 wherein the compound binds to a thrombus site.
- 21. (amended) The reagent of Claim 1 the compound binds to a site of an infection.
 - 34. A peptide comprising

a biological-function domain which causes the peptide to localize at a target site, and

a metal ion-binding domain which comprises the sequence Gly-Gly-Z or Gly-Gly-Gly-Z wherein Z is selected from the group consisting of cysteine, homocysteine,

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isocysteine, penicil amine, 2-mercaptoethylamine, 3-mercaptopropylamine and D-stereoisomers thereof.

- 35. A peptide according to claim 34 in which the metal ion-binding domain further comprises a radioactive metal ion coupled thereto.
- 36. A method for radiolabeling a peptide with Tc-99m which comprises the steps of (a) reacting a peptide comprising

a biological function domain which cause said peptide to localize at a target site, and

a metal-ion binding domain which comprises the sequence Gly-Gly-Z or Gly-Gly-Gly-Z wherein Z is selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoethylamine, 3-mercaptopropylamine and and D-stereoisomers thereofor with To 99m ion.

and (b) recovering radiolabeled peptide.

37. A method of detecting at least one of the existence and locus of infection or inflammation in the body of a mammalian subject suspected of suffering from infection or inflammation, the method comprising: (a) administering to said subject a peptide comprising

a biological-function domain which causes the peptide to localize at a target site, and

a metal ion-binding domain which comprises the sequence Gly-Gly-Z or Gly-Gly-Z wherein Z is

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selected from the group consisting of cysteine, homocysteine, isocysteine, penicillamine, 2-mercaptoethylamine, 3-mercaptopylamine and D-stereoisomers thereof,

said peptide bearing a Tc-99m ion which has been coupled to said metal ion-binding domain; and (b) detecting the Tc-99m bearing peptide, and thereby determining the existence and locus of infection or inflammation.

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